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Title: IONTOPHORETIC STUDY OF SPEED OF ACTION OF VARIOUS MUSCLE RELAXANTS

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It has been suggested that the onset time is slower for more potent muscle relaxants [1]. The purpose of this study was to determine the onset and offset times for four relaxants applied directly to the end-plate.

METHODS. All experiments were performed using the frog (Rana pipiens) cutaneous pectoris preparation. Membrane potentials were recorded with microelectrodes inserted intracellularly close to the synapse. Pulses of acetylcholine (ACh) were applied iontophoretically (1-50 nA, 10-100 ms; every 0.5-2.0 s) to the synaptic area from the central barrel of a triple barrelled electrode. Gallamine (GAL), d-tubocurarine (CUR), atracurium (ATR) and doxacurium (DOX) were also applied iontophoretically from one of two other barrels (10-200 nA, 10-200 s). The ACh potentials were measured during onset and offset of the blockade.

RESULTS. The exponential time constants of onset (T_{on}; Fig. 1A) for 47%-56% blockade were (± SD): <0.3 s GAL (n=4); 1.1 ± 0.2 s CUR (n=3); 2.0 ± 0.3 s ATR (n=2); 3.4 ± 0.3 s DOX (n=4). After a pulse of muscle relaxant, recovery from inhibition also proceeded exponentially (Fig. 1B). The time constants of recovery (T_{off}) were (± SD): < 0.4 s GAL; 2.4 ± 0.3 s CUR; 4.4 ± 0.5 s ATR and 7.1 ± 0.4 s DOX. Equilibrium dissociation constants were (μM ± SD): 51.4 ± 4.3 GAL (n=4); 0.59 ± 0.7 CUR (n=3); 0.29 ± 0.2 ATR (n=2) and 0.11 ± 0.3 DOX (n=3).

DISCUSSION. This study shows that relaxants applied directly at the end-plate have different onset and offset time constants. The time constants (GAL<CUR<ATR<DOX) are directly related to the potency of the drug.

REFERENCE.
1. Bowman et al., Anesthesiology 69: 57-62, 1988.

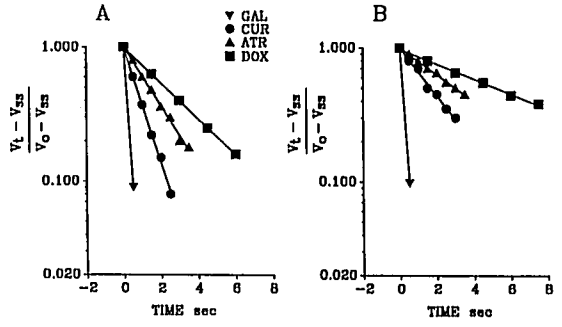

FIGURE.
1. Onset (A) and offset (B) of action of different relaxants.

A811

TITLE: **DOUBLE BURST CHARACTERISTICS OF MUSCLE RELAXANTS IN CHILDREN.**

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Introduction: Double burst stimulation (DBS) has been shown to allow easier recognition of fade than train-of-four (TOF) stimulation.[1] Since muscle relaxants produce different degrees of fade at the same depth of paralysis,[2] we hypothesized that the sensitivity of DBS may be drug-related. To test this hypothesis, the relationship between the intensity of neuromuscular blockade and the ability of the clinician to detect DBS and TOF fade was studied during recovery of paralysis with pancuronium, atracurium and vecuronium.

Methods: With institutional approval, 11 unpremedicated ASA I or II children, 2-10 years of age, scheduled for elective surgery were randomly assigned to receive pancuronium 0.15 mg/kg, atracurium 0.5 mg/kg or vecuronium 0.15 mg/kg iv. Anesthesia was induced with thiopentone 5 mg/kg, atropine 0.02 mg/kg and diazepam 0.2 mg/kg. Percutaneous supramaximal TOF stimuli were applied to the ulnar nerve with a Datex NMT monitor and a reference integrated evoked electromyogram (IEEMG) was obtained from the hypothenar eminence. The muscle relaxant was given and the trachea intubated. Anesthesia was maintained with 70% N_2O in O_2, and increments of fentanyl 1-2 μg/kg. Ventilation was controlled to maintain normocapnia. To assess depth of paralysis, TOF stimuli were applied to the ulnar nerve every 20 s during spontaneous recovery of the neuromuscular blockade, and the hypothenar IEEMG's were recorded. The ulnar nerve of the other extremity was stimulated in random sequence with DBS and TOF, 15 s apart. The responses were evaluated manually by one investigator who was blinded to the muscle relaxant and to the TOF ratio. The frequency of detectable fade was determined for each mode of stimulation at the TOF intervals shown in the table. Chi-squared analysis with Yates correction, and Fisher exact test where appropriate, were applied to determine significant differences ($p<0.05$) in the frequencies.

Results: 269 paired responses were assessed in 11 children. DBS fade was detected over a range of TOF intervals that was greater for pancuronium and atracurium than for vecuronium (Table). DBS improved recognition of fade compared to TOF (Table). Fade of the IEEMG increased in the order vecuronium < atracurium < pancuronium. TOF ratios (means ±SD) at 50% reduction in the amplitude of IEEMG (TOF $ratio_{50}$) were significantly greater for vecuronium (0.37 ± 0.15) than for atracurium (0.22 ± 0.08) and pancuronium (0.18 ± 0.09).

Discussion: DBS was most useful for the muscle relaxants that produced a high degree of fade during recovery of neuromuscular blockade. For each relaxant, DBS allowed detection of fade over a wider range of paralysis than TOF.

Table: Frequency (%) of detectable fade.

TOF Interval	Pancuronium		Atracurium		Vecuronium	
	DBS	TOF	DBS	TOF	DBS	TOF
0.11-0.20	100	87	100	90	100*	53
0.21-0.30	93*	21	100*	38	80*	27
0.31-0.40	79*	14	89*	8	33	9
0.41-0.50	76*	0	75*	0	20	0
0.51-0.60	62*	0	61*	0	0	0
0.61-0.70	33*	0	14	0	0	0
>0.70	0	0	0	0	0	0

* $p < 0.05$ vs TOF

References: 1. Anesthesiology 73:401-403, 1990
2. Br J Anaesth 52:1111-1114, 1980